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1-(4-Chlorophenyl)-4,4-dimethyl-3-pentanone

CAS # 66346-01-8

HPV Test plan

Bayer CropScience LP

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Executive Summary

Bayer CropScience LP (Bayer) hereby submits for review and public comment their test plan for 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone (CAS# 66346-01-8) under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program.

<u>IUPAC Name</u>	<u>Common Name</u>	<u>CAS#</u>
1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone	HWG alkylketone	66346-01-8

HWG alkylketone is used as an intermediate in the production of an agricultural fungicide.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, Bayer has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. Existing data indicates that this chemical is of high concern for aquatic toxicity, low - moderate concern as Persistent Organic Pollutants (POP), low concern for skin irritation, and low concern for acute mammalian toxicity. In a separate submission as 'Confidential Business Information', Bayer has explained in detail that this substance is a closed-system intermediate and therefore a reduced data set is required. To fulfill the SIDS data set, an "*in vitro* Mammalian Cytogenetic Test" (OECD 473) and Teratogenicity study (OECD 414) on HWG alkylketone is proposed for purposes of the HPV Program is proposed for purposes of the HPV Program.

Closed System Intermediate Chemical Status

A separate document is being submitted to EPA to describe the process, sites, and transport of TCH to explain “closed-system” intermediate status. This information is considered ‘Confidential Business Information’ and therefore is not available to the public in this document.

Data Review

Physicochemical properties:

The properties of HWG alkylketone were available from internal studies, except for the Partition Coefficient which was calculated with EPIWin Modeling Program. HWG alkylketone is liquid at ambient temperatures and has a boiling point of approximately 178 °C. Vapor pressure is less than 0.03 hPa at temperatures from 20 to 55°C. The calculated octanol/water partition coefficient is 3.97 and it is slightly soluble in water (20.7 mg/l at 20°C). Data is available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Environmental Fate:

Photodegradation of HWG alkylketone was calculated at a 16.5 hours half-life. Fugacity modeling demonstrates partitioning to the soil (72.5%) and water (22.3%) compartments. Biodegradation modeling demonstrates that HWG alkylketone is not readily biodegradable. No water stability study has been located. Based on similar compounds and experience, this compound is expected to be extremely stable in water (>1 year at pH 5–9). Although this material is not readily biodegradable, it is not considered to be bioaccumulative. Data is available for all endpoints through modeling. Since this is a closed system intermediate with minimal potential for exposure to the environment, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Ecotoxicology:

Several aquatic studies have been done. LC₅₀ results of 4.9 mg/l (96 hr, *Leuciscus idus*) and 3.74 mg/l (96 hr, *Salmo gairdneri*); and an EC₅₀ of 3.2 mg/l (48 hr, *Daphnia*) indicate that HWG alkylketone is toxic to aquatic organisms. The EcoSAR calculation for Green Algae (96hr) resulted in an EC₅₀ of 2.015 mg/l. Since the EcoSAR estimations are very close to measured results for fish and Daphnia, the EC50 calculation of toxicity to Algae is acceptable. No additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Mammalian Toxicology:

Toxicity studies in animals show that HWG alkylketone is of low acute toxicity by all routes of exposure: oral LD₅₀ = 4748 mg/kg (rat); inhalation LC₅₀ > 2928 mg/m³ (rat); and dermal LD₅₀ > 5000 mg/kg (rat). (See Table 1 and IUCLID document for more detail).

There is a negative Ames study on HWG alkylketone to fill the mutagenicity endpoint. No studies on chromosome aberration were located. An “*in vitro* Mammalian Cytogenetic Test” (OECD 473) on HWG alkylketone is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

There were no repeat dose, fertility, nor developmental studies found. Since HWG alkylketone is a “closed-system intermediate”, the repeat dose and fertility studies are waived. A “Teratogenicity” study (OECD 414) on HWG alkylketone is proposed for purposes of the HPV Program. (See Table 1 and IUCLID document).

“Beyond SIDS” Endpoints:

Studies have been performed to investigate skin and eye irritation. HWG alkylketone was found to be non-irritating to the skin and eyes of rabbits. (See Table 2 and IUCLID document).

Exposure considerations

Since this chemical is used as a closed-system intermediate, there is limited exposure potential to humans, aquatic organisms and the environment. Workers use protective equipment in any situation where accidental exposure is possible. There is no intentional disposal to a wastewater system. With controls imposed, exposure is negligible.

Conclusion

Existing data indicates that this chemical is of high concern for aquatic toxicity, low - moderate concern as Persistent Organic Pollutants (POP), low concern for skin irritation, and low concern for acute mammalian toxicity. In a separate submission, Bayer has explained in detail that this substance is a closed-system intermediate and therefore a reduced data set is required. To fulfill the SIDS data set, an “*in vitro* Mammalian Cytogenetic Test” (OECD 473) and Teratogenicity study (OECD 414) on HWG alkylketone is proposed for purposes of the HPV Program is proposed for purposes of the HPV Program.

Table 1. Available data for HWG ALKYLKETONE

Endpoint	HWG ALKYLKETONE (CAS# 66346-01-8)
Physical-Chemical Data	
Molecular weight	224.75
Physical state	liquid
Melting Point	18 °C
Boiling Point	178 °C
Vapour Pressure	< 0.001 hPa at 20 °C
Partition Coefficient (logP _{ow})	3.97
Water Solubility	20.7 mg/l at 20 °C
Environmental Fate	
Photodegradation	T ½ = 16.5 hrs
Fugacity (distribution)	Air: 1.16 % Water: 22.3 % Soil: 72.5 % Sediment: 3.99 %
Biodegradability	T ½ > 1 year
Water Stability	>1 year at pH 5–9
Ecotoxicology	
Acute Fish Toxicity 96 hrs LC ₅₀	4.9 mg/l (<i>Leuciscus idus</i>)
Acute Invertebrate Toxicity 48 hrs LC ₅₀	3.2 mg/l (<i>Daphnia magna</i>)
Algal Toxicity 144 hrs LC ₅₀	2.0 mg/l (EcoSAR)
Mammalian Toxicology	
Acute Toxicity	LD ₅₀ = 4748 mg/kg bw (oral, male/female rats) LC = > 2928 mg/m ³ (inhalation, 4 hr, rats) LD ₅₀ > 5000 mg/kg bw (dermal, rat)
Mutagenicity	Ames = negative
Chromosome Aberration	No data
Repeated Dose Toxicity	No data
Reproductive Toxicity	No data
Developmental Toxicity	No data

* Robust summaries and References can be found in the IUCLID document.

Table 2. “Beyond SIDS” data for HWG ALKYLKETONE

Endpoint	HWG ALKYLKETONE (CAS# 2231-57-4)
Skin Irritation	Not irritating (4 hrs, rabbit)
Eye Irritation	Not irritating (24 hrs, rabbit)

* Robust summaries and References can be found in the IUCLID document.

Table 3. Test Plan for HWG ALKYLKETONE

Endpoint	Data Availability	Acceptable	Planned testing
Physical-Chemical Data			
Melting Point	✓	✓	
Boiling Point	✓	✓	
Vapour Pressure	✓	✓	
Partition Coefficient (logP _{ow})	✓	✓	
Water Solubility	✓	✓	
Environmental Fate			
Photodegradation	✓	✓	
Fugacity	✓	✓	
Biodegradability	✓	✓	
Water Stability	✓	✓	
Ecotoxicology			
Acute Fish Toxicity	✓	✓	
Acute Invertebrate Toxicity	✓	✓	
Algal Toxicity	✓	✓	
Mammalian Toxicology			
Acute Toxicity	✓	✓	
Mutagenicity	✓	✓	
Chromosome Aberration			<i>OECD 473 in vitro</i>
Repeated Dose Toxicity	Not required 'Closed system intermediate'		
Reproductive Toxicity	Not required 'Closed system intermediate'		
Developmental Toxicity			<i>OECD 414</i>

✓ = data available and considered adequate.